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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,280	12/10/2001	Frank Himmelsbach	5/1262	7351

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EXAMINER
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PATEL, SUDHAKER B

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/016,280

Applicant(s)

HIMMELSBACH ET AL.

Examiner

Sudhaker B. Patel, D.Sc.Tech.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☒ Claim(s) 8-11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

Applicants' communication paper # 7 dated 6/4/03 is acknowledged.

#### *Election/Restrictions*

1. Because applicants did not distinctly and specifically point out the supposed errors in the restriction/election requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Applicants have elected species of generic Formula (I) of claim 1, namely, compound of Example 3 recited in page 44 lines 20-22 (= 4-[(3-Chloro-4-fluorophenyl)amino]-6-[[4-(N,N-diethylamino)-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline), claims (in part) 1-11, drawn to compounds, compositions, method of use, and the first recited process of making the same for the generic Formula (I).

Applicants are reminded of the election of species guidelines provided in MPEP 803.02, which are followed for the examination.

The elected species of compound of Example 3 as stated earlier has following meanings for variables in the generic Formula (I) of claim 1:

X	= N;
A	= imino(= -NH-);
B	= -CO-;
C	= 1,2-vinylene( = -CH=CH-);
D	= methylene (= - CH <sub>2</sub> -);
E	= diethylamino;
Ra	=H;
Rb	=phenyl substituted by R1 = H, R2 = F, in 4 position of phenyl, and R3 = Cl in 3-position of phenyl;
Rc	=-O-(alkyl)-cycloalkyl (= cycloalkyl-alkoxy-).

Initial search with above definitions of the variables for the species did reveal prior art(s). Therefore, the search was limited to meanings of variables as stated above. All other definitions of variables than stated above are excluded from further consideration. 37 CFR 1.142(b).

This application has been found to contain more than one invention. Therefore, the requirement is still deemed proper and is therefore maintained.

First action on merits follows.

**2.** *Priority*

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.
2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Germany on 6/21/1999. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter.

3. It is noted that this application appears to claim subject matter disclosed in prior Application No. 60146644, filed 7/30/1999. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on

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which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

***Specification***

**3.** The disclosure is objected to because of the following informalities: The continuity information recited as :” This application is a 371 of PCT/EP00/05547 filed 6/21/1999” is not proper. The Office record for this application does not indicate the relationship between the above stated applications, namely, the U.S. Provisional Application Sr. No. 60/14664 filed 7/30/199; The PCT/EPOO/05547 filed 6/21/1999; DE 19928281.1 filed 6/21/1999, and DE10023 085.7 filed 5/11/2000.

Appropriate correction is required.

***Claims objections***

**4.** Claims 8-11 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim 7. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

***Claim Rejections - 35 USC § 112***

**5.** The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A). Claims 1-5 recite: "Bicyclic heterocycles of general Formula: Correction to A quinqzoline compound of Formula". Is required.

(B). Claims 1-5 recite (where applicable) at the end of the claims: "the tautomets, stereoisomers and salts there of". Such recitation includes other compounds/mixtures those are not claimed. Correction to: "or the tautomers, or stereoisomers or pharmaceutically acceptable salts thereof" is required.

(C). Claim 6 recites specific compounds and is ending as : "as well as the salts thereof". It is not very clear as to what applicants want to claim. The recitation includes mixture of compound also. Correction to : "or pharmaceutically acceptable salts thereof" is required.

(D). Claim 7 recites: "Physiologically acceptable salts of the compounds... to at least one of claims ....". Correction to Pharmaceutically acceptable salts of the compounds of claims 1 to 6..." is required.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barker A. J. ( EP 566226, also cited as Chemical Abstract DN 120:217715) as applied to claims above, and further in view of Bridges et al ( WO 9738983).

Applicants are claiming substituted quinazolines, pharmaceutical compositions, and their use as inhibitors of Tyrosine kinase for treating diseases consisting of tumoral diseases, diseases of lungs and respiratory tract and others.

Ref. '226 is teaching making of quinazoline tyrosine kinase-inhibiting anticancer agents.

The ref. '226 chemical core is:

4,6-Quinazolinediamine, 7-methoxy-N-4-(3methylphenyl). See compound having CAS RN # 153437-18-4.

The ref. '226 differs from the instant claims by having CH<sub>3</sub>-O- instead of -O-CH<sub>2</sub>-Cycloalkyl, and -NH<sub>2</sub> instead of -NH-CO-CH=CH-CH<sub>2</sub>-N(alkyl)<sub>2</sub>.

The other ref. '983 teaches making of irreversible inhibitors of tyrosine kinase. See compound of Example 55 on page 123, and the compounds of claim 1. on pages 152-154.

The ref. '983 teaches modification(s) of the 6-NH<sub>2</sub> group to -NH-CO-CH=CH-CH<sub>2</sub>-N(alkyl)<sub>2</sub> or NH-CO-CH=CH-CH<sub>2</sub>-NH<sub>2</sub> or NH-CO-CH=CH-CH<sub>2</sub>-NH(alkyl) as claimed herein.

However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference. 'Barker i.e. substituted quinazoline with free 6-NH<sub>2</sub> and condense with maleic anhydride to get -NHCO-CH=CH-COOH, and modify the end group as taught by ref. ' 983 because an ordinary artisan would have the reasonable expectation that any of the species of the genus would have similar properties, and thus, the same use as the genus as a whole.

The 4-phenyl-substituted quinazoline derivatives were known prior to 6/21/1999.

Also modification of 6-NH<sub>2</sub> group on to quinazolines were known, and compounds so obtained are having pharmacological activity as inhibitors of Tyrosan Kinase.. This pharmaceutical activity has been retained by compounds of both of the references.

It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within the genus. In re Susi, 440 F.2d 442, 445, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in Mark & Co. V.s. Biocraft Laboratories, 874 F.2d 804, 10 USPQ 2d 1943, 1846 (Fed. Cir. 1989).

Applicants are claiming their compounds as novel. However, they are differing by having cycloalkyl instead of alkyl substitution on to 7-OH group of quinazoline and such compounds involve close structural similarity with the prior art(s) as cited above. The 6-membered N-contain ring will provide isomers with 2 N atoms participating with a double bond either between themselves or with adjacent carbon atom(s). Applicants have not shown that their novel useful compounds, which are structurally similar to prior art(s), possessed some unobvious or unexpected beneficial property not possessed by the prior art compound(s). In re Norris (CCPA 1950) 179 F2 970, 84 USPQ 458.


**Conclusion**


7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is 703 308 4709.

The examiner can normally be reached on 6:30 to 5:00 pm (Monday-Thursday). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on 703 308 4716 or Sr. Examiner Mr. Richard Raymond at (703) 308 4523.

The fax phone numbers for the organization where this application or proceeding is assigned are 703 308 4556 for regular communications and 703 308 4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.

  
Sudhaker B. Patel, D.Sc.Tech.  
July 1, 2003.

  
MUKUND SHAH  
SUPERVISORY PATENT  
EXAMINER  
ART UNIT 1624